CERTIFICATE OF MAILING

I hereby certify that the enclosed Brief on Appeal is being depositied with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner of Patents and Trademarks, Washington DC.

James L Rowe

Date: 3-7-06 JamesL. Rowe

GAU 1614

IN THE UNITED STATES PATENT AND TRADEMARD OFFICE

Appellant: Howard L. Elford

Serial No. 09/123,620

Filed: 7/28/98 Group Art Unit: 1614

THERAPEUTIC PROCESS FOR INHIBITING NF-$_k$B EXAMINER: K. FONDA

Docket No. HEBVR-5

Commissioner of Patents and Trademarks

Washington DC 20231

BRIEF ON APPEAL TRANSMITTAL LETTER

Accompanying this Transmittal Letter sre three copies of the Brief on Appeal in the matter of the above-entitled application. A timely request for extension of time has been filed. The requisite filing fee of $150 is enclosed, Appellant having been granted Small Entity satus.

Respectfully submitted,

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Howard L. Elford

Serial No. 09/123,620

Filed: 7/28/98 Group Art Unit 1614

THERAPEUTIC PROCESS FOR Examiner K. Fonda

INHIBITING NF-kB

Docket No. HEBVR-5

Commissioner of Patents and Trademarks

Washington DC 20231

BRIEF ON APPEAL

1. The above-entitled application will be assigned to Molecules For Health, Inc. 3313 Gloucester Road, Richmond VA 23277. The inventor in the matter of the above-entitled application is the principal stockholder of that small entity corporation.

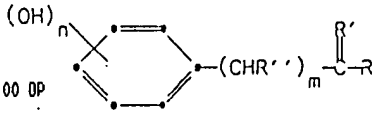
2. There are no related appeals or interferences.

3 STATUS OF CLAIMS

Claims 1-11 have been finall rejected and are under appea;

4. SUMMARY OF THE INVENTION

This invention provides a therapeutic process for the inhibition of NF-kB in whose cells NF-kB has been activated , which process coprises administering to a mammal in whose cells NF-kB has been activated and who is in need of treatment, an NF-kB inhibitory amount of a free radical inhibiting amount of a compound of the structure



wherein n is 2-5, m is 0 or 1,R is NH , NHOH, OC_1-alkyl or O-phenyl, R' is O, NH or NOH, R" is H or OH, acylated phenol derivatives of said drugs and pharmaceutical-acceptable acid-addition thereof. There are also claims to an identical

process wherein the NF-κB inhibitor is a free-radical scavenger or is a ribonucleotide reductase inhibitor.

5. **CONCISE STATEMENT OF THE ISSUES FOR REVIEW**

All claims are rejected under 35 U.S.C. 112, 2nd para. as being indefinite for failing to particularly point out and distinctly claim the invention on the ground that the phrase "NF-κB inhibiting amount" has not been adequately defined in the specification.

All claims are rejected as obvious in view of Van't Riet et al U.S.Patent4,623,659.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. 112 2nd PARA.

Claims 1-11 are rejected under 35 U.S.C. 112, 2nd paragraph for using the term "NF-κB inhibiting amount" on the grounds that the term has no particular art-recognized meaning and has not been adequately defined. Appelant has reviewed the prior art cited in the 'CITATION OF ART' and finds that the following references had specific directions for activating NF-κB and for carrying out experiments to see whether certain compounds could inhibit the activation: AR, AS, AT, AU, AV, AB and AZ. In addition the references cited contain numerous references to the related prior art as does the review article, Ref. BF. Appellant does not believe that it was incumbent upon him to place in the specification subject matter that was well-known to those skilled in the art to which it pertains. A skilled artisan would follow the directions in the prior art for activating NF-κB and would follow standard procedures for determining whether known compounds could inhibit this activation. Nothing is discerned herein which would make it

difficult for one of even ordinary skill in the art to carry out the required determinations. Appellant submits that the determination of the amount of a compound needed to inhibit the activation of NF-κB can be readily determined by following the teachings of this specification and of the cited prior art and need not be further defined.

In further support of Appellant's position that it is not necessary to encumber a specification with information that is readily available to the skilled practioner, is the fact that the Examiner was able to find several references showing procedures for the activation of NF-κB and for determining wheter certain compounds could inhibit this process and to what degree. These references were cited by the Examiner in support of a rejection of the claims under 35 U.S.C. 103(A). Surely, if such references rendered Appellant's invention obvious, they would be similarly available to any skilled practitioner wishing to determine whether his (or her) compounds had similar inhibiting activity,

The rejection of the claims under 35 U.S.C. 112 2nd para. was not well taken and, in view of the above arguments, should be withdrawn.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. 103 (a)

Claims 1-11 are rejected as obvious under 35 U.S.C. 103(a) over VAN't Riet et al on the ground that the compounds disclosed therein are known to be Ribonuckeotide Reductase Inhibitors (RRI's) and free-radical scavengers. It is the Examiner's opinion that any RRI must of necessity be an anti-oxidant and that anti-oxidants are known to inhibit NF-κB. However, The Examiner goes on to say, without citing any reference, that one of ordinary skill in the art would recognize that RRIs and free radical scavengers are also all anti-oxidants. It should be

noted that enzymes like ribonucleotide reductase can be destroyed or their action inhibited by means other thAn oxidation. What if ribonucleotide reductase acts by initiating a free-radical reaction and the Van't Riet et al compounds are free-radical-scavengers. Or perhaps they act by combining with the surface of the reductase at sites which are necessary for reaction with a ribonucletide?

Before stating Appellant' position in this matter, Appellant would like to summarize certain aspects of free.radical chemistry which are involved in the claimed processes. There are two ways of blocking a free-radical reation. First, destroy rhe compound which initiates the reaction-here, a hydroperoxide. Alternatively, a free-radical inhibitor can be added to the reaction mixture to end the free-radical chain. For example, in making BUNA-S, a free radical reaction is started by addition of a peroxide to the mixture of styrene and butadiene. When the reaction has progressed sufficiently far to give a rubber of the desired characteristics, a free-radical scavenger is added to stop th epolymerization from proceding further. In the instant case, the Examiner's anti-oxidant compounds all destroy the peroxide initiator, whereas Appellant's free-radical scavengers all attack and stop the chain reaction.

In order to bolster his rejection, the Examiner has cited a paragraph from page 42 of Casarett & Doull's Toxcology, Fifth Edition which reads as follows:"Peroxidase free-radicals are eliminated by electron transfer to glutathione, which is reversed by NAPDH-dependant glutathione reductase. Thus, glutathione plays an important part in the detoxification of both electrophiles and free-radicals". The Examiner then states that "a compound which is the inhibitor of a reductase, or a

free-radical scavenger, must necessarily be an oxidizing agent". In a free-radical chain reaction, the free-radical has an extra electron which it transfers to a substrate and thus accomplishs a one-electron oxidation of the substrate. This new free-radical becomes a one eiectron oxidizing agent in its own right and so on till the chain reaction is terminated. It is thus apparent that the substrate is a one-electron reducing agent. It is, however, Appellant's position that to use the term "anti-oxidant" when referring to free-radicl chain reactions and one-electron transfers is to torture the accepted meaning of "anti-oxidant" beyond recognition. Anti-oxidants prevent the reaction of oxygen, peroxides etc with substrates. These reactions all involve two-electron transfers which permanently, and not transitorially, change the oxidation state of the compound being oxidized.

As can be seen from the above arguments, Appellant's claimed free-radical scavengers do not actually "oxidize" anything. They have the ability to terminate a free-radical chain reaction, and nothing more.

Appellant submits that the rejection of the claims under 35 U.S.C. 103(a) has been overcome by the above arguments and should be withdrawn.

CONCLUSION

Appellant subits that the rejection of the claims under 35 U.S.C. 112 paragraph 2 was not founded upon the factual situation regarding procedures available in the cited prior art for activating and inhibiting NF-kB Thus the rejection should be withdrawn.

Appellant has also demonstrated by argument, that the rejection of the claims under 35 U.S.C. 103(a) was based upon a tortured use of the term "anti-oxidant" so that the cited prior art encompassed Appellant"s claims and that this farfetched application of the term oxidation was made with the use of hindsight based upon Appellant's own disclosures,

Allowance of the claims is repectfully requested.

Respectively submitted,

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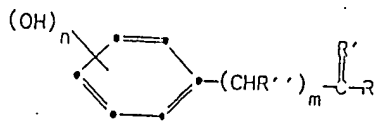
Date: 3-7-00

ADDENDUM

CLAIMS ON APPEAL

1) A process for inhibiting NF-κB in a mammalian cell in which NF-κB has been activated by an agency external to said cell which comprises administering to the mammal in whose cells NF-κB has been activated an NF-κB inhibiting amount of a drug represented by the formula



wherein n is 2-5, m is 0 or 1, R is NH, NHOH, OC_{1-3} alkyl or O-phenyl, R' is O, NH or NOH, and R" is OH, acylated phenol derivatives of said drugs, and pharmaceutically-acceptable acid-addition salts thereof.

2) A process according to Claim 1 in which the external agency activating NF-κB in an inflammatory process includes, but is not limited to, a cytokine, an activator of protein kinase B, a virus or an oxidant.

3) A process according to Claim 1 in which the external agency activating NF-κB is a drug or radiation administered to the host mammal in a chemotherapeutic process used in the treatment of cancer.

4) A process according to Claim 1 in which the administered NF-κB inhibitor is a free-radical scavenger.

5) A therapeutic process according to Claim 1 in which the NF-κB inhibitor is N,3,4-trihydroxybenzamide.

6) A therapeutic process according to Claim 1 in which the NF-κB inhibitor is N,3,4,5-terahydroxybenzamide.

7) A therapeutic process according to Claim 1 in which the NF-κB inhibitor is N, 3,4-tetrahydroxybenzimideamide.

8) A therapeutic process according to Claim 1 in which the NF-$_k$B inhibitor is a ribonucleotide reductase inhibitor.

9) A process according to Claim 1 in which the external agency activating NF-$_k$B is the reslt of a tissue transplant, an organ transplant or a cell transplant in a mammal.

10) A process according to Claim 1 in which the external agency activating NF-$_k$B is arteriosclerosis.

11) A process according to Claim 1 in which the external agency activating NF-$_k$B is diabetes.